wherein R^N is any aryl or heteroaryl group and Z^N is $(CO)_{mm}$-X^N_{nn}-Y^N_{oo};
wherein mm, nn, oo are 0 or 1 and X^N,Y^N are NH, NR^{NN}, O or CH_2;
wherein R^{NN} is a C_1 – C_{12} alkyl group.

REMARKS

Applicants thank the Examiner for the withdrawal of the previous claim rejections under 35 USC § 112, second paragraph, and 35 USC § 102(a). Applicants also thank the Examiner for the cordial telephone conversation with the undersigned agent on December 17, 2002. In that conversation, the Examiner confirmed that claims 12, 15, and 26, previously withdrawn from consideration, were back in the case. Also, various minor amendments to certain claims, described below, were discussed.

Claims

Claims 11, 13 to 20, 22, 24, 26, 28, and 33 to 42 are in the case. Claims 33 to 40 have been allowed. In the instant Amendment claim 12 has been cancelled and claims 11, 13, 14, 15, 24, 26, 28, 41, and 42 have been amended as described below. All amendments are shown on the attached sheets entitled "Version With Markings to Show Changes Made". No new matter has been entered.

Claim Objections

In response to the Examiner's objection to claim 13 concerning use of parentheses throughout the claim, claim 13 has been amended as follows. In the paragraph beginning with "where A is selected from", three sets of parentheses have been deleted, and, in place of the second closed parenthesis, a comma has been inserted (please refer to the Version With Markings to Show Changes Made). This follows telephone discussion with the Examiner on December 17, 2002.

Also as discussed with the Examiner on December 17, 2002, claims 11, 14, 15, 41, and 42 have been amended by deleting the hyphen at the end of the term "R^N-Z^N-", such that the term now reads --R^N-Z^N--.

Rejections Under 35 USC § 112, Second Paragraph

Claims 11 to 20, 22, 24, 26, 28, 41, and 42 were rejected under 35 USC § 112, second paragraph, as indefinite.

In particular, claims 11 and 12 were rejected for reciting "formula I", for which recitation there was allegedly no antecedent basis. In the instant amendment claim 12 has been cancelled and

claim 11 has been amended to recite --formula Ia--, rather than "formula I", corresponding to formula Ia appearing in the claim. The same amendment has been effected in claim 15.

Claim 13 was rejected on the grounds that the recitation "containing carbonyl linkages (C=O, C=S, C=NOH)" was indefinite. In the instant amendment claim 13 has been amended to recite --containing carbonyl linkages selected from the group consisting of C=O, C=S, and C=NOH--, as suggested by the Examiner.

Claims 11, 12, 14, 15, 41, and 42 were rejected on the grounds that the recitation "wherein R^{NN} is a short chain alkyl group (C_1 - C_{12})" rendered the claims indefinite. In the instant amendment, claims 11, 14, 15, 41, and 42 have been amended to recite --wherein R^{NN} is a C_1 - C_{12} alkyl group--, as suggested by the Examiner. As noted above, claim 12 has been cancelled.

Applicants have also amended the dependencies of claims 15, 24, 26, and 28, in view of the cancellation of claim 12. Accordingly, claim 15 now depends from claim 11, and claims 24, 26, and 28 no longer depend from claim 12.

Finally, claim 15 has been further amended to recite $-F^1-$, $-F^2-$, $-G^1-$, and $-G^2-$, rather than "F_1", "F_2", "G_1", and "G_2", in accordance with claim amendments effected in Applicants' previous Amendment and Response.

Applicants submit that all pending claims are now in condition for allowance, and look forward to receiving a Notice of Allowability in the near future.

If the Examiner has any questions about the instant Amendment and Response or the application, she is asked to please telephone the undersigned agent or Carol Miernicki Steeg (Reg. No. 39,539) at 613-533-2342.

Please charge any fees that may be required, for which no cheque is enclosed, to Deposit Account No. 17-0110.

Respectfully submitted,

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Date: 18 Dec 2002

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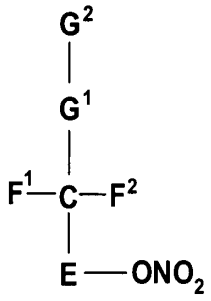
VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE CLAIMS:

Claim 12 has been cancelled and claims 11, 13, 14, 15, 24, 26, 28, 41, and 42 have been amended as follows:

11. (Twice amended) A method for providing sedation, mitigating anxiety or providing anaesthesia in a subject in need thereof, comprising administering to a subject an effective amount of a therapeutic compound, wherein the therapeutic compound is of the formula (Ia):

(Ia)



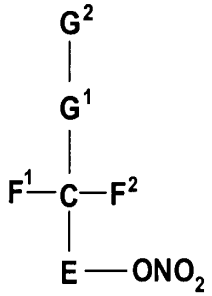
in which F^2 is an organic radical which may be joined in a cyclic ring system with G^2, and which may contain inorganic counterions, but is not a nitrate group; E is a methylene group and G^1 is a methylene group or does not exist; F^1 is H; and G^2 is R^N-Z^N[-];

wherein R^N is an organic radical possessing a heteroaryl group containing P or S atoms where said P or S are positioned β, γ, or δ to a nitrate group as identified in formula Ia; and Z^N is W^N_{mm}-X^N_{nn}-Y^N_{oo};

wherein mm, nn, oo are 0 or 1 and W^N, X^N, Y^N are NH, NR^{NN}, CO, O or CH_2;

wherein R^{NN} is a [short chain] C_1 - C_{12} alkyl group [(C_1 - C_{12})].

13. (Twice amended) A method for providing sedation, mitigating anxiety or providing anaesthesia in a subject in need thereof, comprising administering to a subject an effective amount of a therapeutic compound, wherein the therapeutic compound is of the formula (Ic):

(Ic) 

in which E is $(R^1R^2C)_m$ and $G^2–G^1–CF^1F^2–$ is $R^{19}–(R^3R^4C)_p–(R^{17}R^{18}C)_n–$;

wherein: m, n, p are integers from 0 to 10;

$R^{3,17}$ are each independently hydrogen, a nitrate group, or A; and

$R^{1,4}$ are each independently hydrogen, or A;

where A is selected from a substituted or unsubstituted aliphatic group [(]comprising a branched or straight-chain aliphatic moiety having from 1 to 24 carbon atoms in the chain, which optionally may contain O, S, NR^6 and unsaturations in the chain, optionally bearing from 1 to 4 hydroxy, nitrate, amino, aryl, or heterocyclic groups; an unsubstituted or substituted cyclic aliphatic moiety having from 3 to 7 carbon atoms in the aliphatic ring, which optionally may contain O, S, NR^6 and unsaturations in the ring, optionally bearing from 1 to 4 hydroxy, nitrate, amino, aryl, or heterocyclic groups; an unsubstituted or substituted aliphatic moiety constituting a linkage of from 0 to 5 carbons, between R^1 and R^3 and/or between R^{17} and R^4, which optionally may contain O, S, NR^6 and unsaturations in the linkage, and optionally bearing from 1 to 4 hydroxy, nitrate, amino, aryl, or heterocyclic groups[)]; a substituted or unsubstituted aliphatic group [(]comprising a branched, cyclic or straight-chain aliphatic moiety having from 1 to 24 carbon atoms in the chain[)], containing carbonyl linkages selected from the group consisting of [(]C=O, C=S, and C=NOH[)], which optionally may contain O, S, NR^6 and unsaturations in the chain, optionally bearing from 1 to 4 hydroxy, nitrate, amino, aryl, or heterocyclic groups; a substituted or unsubstituted aryl group; a heterocyclic group; an amino group selected from alkylamino, dialkylamino, cyclic amino, diamino and triamino moieties, arylamino, diarylamino, and alkylarylamino; hydroxy; alkoxy; a substituted or unsubstituted aryloxy;

wherein X is F, Br, Cl, NO_2, CH_2, CF_2, O, NH, NMe, CN, NHOH, N_2H_3, $N_2H_2R^{13}$, $N_2HR^{13}R^{14}$, N_3, S, SCN, $SCN_2H_2(R^{15})_2$, $SCN_2H_3(R^{15})$, $SC(O)N(R^{15})_2$, $SC(O)NHR^{15}$, SO_3M, SH, SR^7, SO_2M, $S(O)R^8$, $S(O)_2R^9$, $S(O)OR^8$, $S(O)_2OR^9$, PO_2HM, PO_3HM, PO_3M_2, $P(O)(OR^{15})(OR^{16})$, $P(O)(OR^{16})(OM)$, $P(O)(R^{15})(OR^8)$, $P(O)(OM)R^{15}$, CO_2M, CO_2H, CO_2R^{11}, C(O), $C(O)R^{12}$, $C(O)(OR^{13})$, PO_2H, PO_2M, $P(O)(OR^{14})$, $P(O)(R^{13})$, SO, SO_2, $C(O)(SR^{13})$, SR^5, SSR^7 or SSR^5;

Y is F, Br, Cl, CH_3, CF_2H, CF_3, OH, NH_2, NHR^6, NR^6R^7, CN, NHOH, N_2H_3, $N_2H_2R^{13}$, $N_2HR^{13}R^{14}$, N_3, S, SCN, $SCN_2H_2(R^{15})_2$, $SCN_2H_3(R^{15})$, $SC(O)N(R^{15})_2$, $SC(O)NHR^{15}$, SO_3M, SH, SR^7, SO_2M, $S(O)R^8$, $S(O)_2R^9$, $S(O)OR^8$, $S(O)_2OR^9$, PO_2HM, PO_3M_2, $P(O)(OR^{15})(OR^{16})$, $P(O)(OR^{16})(OM)$, $P(O)(R^{15})(OR^8)$, $P(O)(OM)R^{15}$, CO_2M, CO_2H, CO_2R^{11}, $C(O)R^{12}$, $C(O)(OR^{13})$, $C(O)(SR^{13})$, SR^5, SSR^7 or SSR^5, or does not exist;

R^2, R^5, R^{18}, R^{19} are optionally hydrogen, A or X-Y;

R^6, R^7, R^8, R^9, R^{11}, R^{12}, R^{13}, R^{14}, R^{15}, R^{16} are the same or different alkyl or acyl groups containing 1-24 carbon atoms which may contain 1-4 ONO_2 substituents; or C_1 - C_6 connections to R^1 – R^4 in cyclic derivatives which may contain 1-4 ONO_2 substituents; or are each independently hydrogen, a nitrate group or A;

M is H, Na^+, K^+, NH_4^+, $N^+H_kR^{11}{}_{(4-k)}$ where k is 0-3; or other pharmaceutically acceptable counterion;

and with the proviso that when m = n = p = 1 and R^{19}, R^2, R^{18}, R^1 = H and R^{17}, R^3 are nitrate groups, R^4 is not H.

14. (Twice amended) The method of claim 11, wherein F^2 is a nitrate group; and E, F^1, G^1, G^2 are the same or different organic radicals which may be joined in cyclic ring systems, and which may contain inorganic counterions;

with the proviso that when E and G^1 are methylene groups and F^1 is H, G^2 is not a nitrate group, nor R^N-Z^N[-];

wherein R^N is any aryl or heteroaryl group and Z^N is $(CO)_{mm}$-$X^N{}_{nn}$-$Y^N{}_{oo}$;

wherein mm, nn, oo are 0 or 1 and X^N,Y^N are NH, NR^{NN}, O or CH_2;

wherein R^{NN} is a [short chain] $\underline{C_1 - C_{12}}$ alkyl group [(C_1 – C_{12})].

15. (Amended) The method of claim [12] 11, wherein [F_2] $\underline{F^2}$ is a nitrate group; E and [G_1] $\underline{G^1}$ are methylene groups; [F_1] $\underline{F^1}$ is H; and [G_2] $\underline{G^2}$ is R^N-Z^N[-];

wherein R^N is an organic radical possessing an heteroaryl group containing P or S atoms where said P or S are positioned β, γ, or δ to a nitrate group as identified in formula $\underline{Ia}$; and Z^N is $W^N{}_{mm}$-$X^N{}_{nn}$-$Y^N{}_{oo}$;

wherein mm, nn, oo are 0 or 1 and W^N, X^N, Y^N are NH, NR^{NN}, CO, O or CH_2;

wherein R^{NN} is a [short chain] $\underline{C_1 - C_{12}}$ alkyl group [(C_1 – C_{12})].

24. The method of any one of claims 11, [12,] 13, 14 or 15, further comprising administering the therapeutic compound with a pharmaceutically acceptable vehicle.

26. The method of any one of claims 11, [12,] 13, 14 or 15, wherein the therapeutic compound modulates levels of the cyclic nucleotides cGMP and/or cAMP in said subject.

28. The method of any one of claims 11, [12,] 13, 14 or 15, wherein the therapeutic compound modulates guanylyl cyclase activity in said subject.

41. (Amended) The method of claim 13, wherein when E and G^1 are independently methylene groups or do not exist and F^1 is H, G^2 is not R^N-Z^N[-];

wherein R^N is any aryl or heteroaryl group and Z^N is $(CO)_{mm}$-X^N_{nn}-Y^N_{oo};

wherein mm, nn, oo are 0 or 1 and X^N,Y^N are NH, NR^{NN}, O or CH_2;

wherein R^{NN} is a [short chain] $\underline{C_1 - C_{12}}$ alkyl group [$(C_1 - C_{12})$].

42. (Amended) The method of claim 41, wherein F^2 is a nitrate group; and E, F^1, G^1, G^2 are the same or different organic radicals which may be joined in cyclic ring systems, and which may contain inorganic counterions;

with the proviso that when E and G^1 are methylene groups and F^1 is H, G^2 is not a nitrate group, nor R^N-Z^N[-];

wherein R^N is any aryl or heteroaryl group and Z^N is $(CO)_{mm}$-X^N_{nn}-Y^N_{oo};

wherein mm, nn, oo are 0 or 1 and X^N,Y^N are NH, NR^{NN}, O or CH_2;

wherein R^{NN} is a [short chain] $\underline{C_1 - C_{12}}$ alkyl group [$(C_1 - C_{12})$].